Notes on COVID-19

Part 11: 2020-06-18 to 2020-06-30

Peter Bernard Ladkin
2020-06-30

2020-06-18 According to TheG's Mattha Busby, the UK Scientific Advisory Committee on Nutrition (SACN) is considering Vitamin D and acute respiratory tract infection, and NICE is conducting a "rapid" review of evidence on Vitamin D with support from Public Health England (PHE). Vitamin D is known to enhance the immune system in some ways. 10mg Vitamin D per day is already recommended by PHE "to maintain bone and muscle health". https://www.theguardian.com/world/2020/jun/17/uk-ministers-order-urgent-vitamin-d-coronavirus-review The incidence and severity of Covid-19 amongst BAME people in the UK is notable, and some are wondering about a possible connection with lower levels, even deficient levels, of Vitamin D. Professor Adrian Martineau of Queen Mary College, Uni London is concerned about the lack of research into Vitamin D levels and Covid-19 and is leading a study. Notes Part 8 on 2020-05-30 noted an Indonesian study, and Notes Part 7 on 2020-05-23 referred to an article by Fiona Mitchell in The Lancet Diabetes and Endocrinology on what is known about Vitamin D and respiratory infection https://www.thelancet.com/journals/landia/article/PIIS2213-8587(20)30183-2/fulltext Me, as of today I'm doing what PHE recommends (for other reasons), which is popping 10µg/day of Vitamin D supplement.

2020-06-18 Outbreaks come home. In Bielefeld, in the last three and a half weeks we have only had four new infections. With a third of a million residents, that is a pretty low number. Just over 400 total since the outbreak began; 5 people have died. There was an outbreak in early May (noted in news here on 4th May) in a meat processing plant (slaughterhouse) in Coesfeld near Münster, a city some 60km away across country that is famous for being one of the sites of the Peace of Westfalia agreement in 1648. The local newspapers spoke of working conditions – cold temperatures, which the virus "likes", and imported workers living in close quarters in dormitories. Just down the road, in Rheda-Wiedenbrück, just over 25km away, in the Gütersloh district next to Bielefeld, is an enormous slaughterhouse and processing plant belonging to the family Tönnies, one of the largest if not the largest in Europe. The company had reacted to the Coesfeld outbreak by instituting its own in-house Covid-19 testing centre. On Tuesday 2020-06-16, I looked at the Dashboard maintained by the Robert Koch Institute using the Johns Hopkins system, and noticed that Kreis (district) Gütersloh was one of three yellow districts in Germany (there was also a red district near München). Andrea and I had visited the Botanical Garden in Gütersloh on Sunday, and one of the two farm stores I visit is just up the road also in Kreis Gütersloh, so I felt motivated to find out what was up. It didn't take long. Tönnies had an outbreak. Yesterday, it hit the news. I have written up the Tönnies outbreak in a separate note. Over 1,550 workers were infected at the plant, which employs 6,500 or nearly 7,000 people depending on which newspaper one reads. Almost two-thirds of the workers in the meat cutting part were infected. A lockdown was imposed on the district of Gütersloh, where the plant is located, in accordance with criteria agreed at the Federal level during the relaxation of lockdown conditions some weeks ago – but a week after the outbreak was discovered, even though it was immediately clear that the criteria for reimposing lockdown were fulfilled. Some good news is that, of Saturday 27th June, over 8,000 thousand residents of the district who are not Tönnies workers or family were tested for Covid-19 in the week+ after the outbreak became known, and of the just over 4,000 results in, only nine people have tested positive (NW, paywall). This is what one might expect anywhere, namely that there are a few asymptomatic cases, and people are hoping that it shows the Tönnies outbreak has not spread into the wider population. We'll see. A huge piece of luck if so. On a less-good note, about a fifth of Tönnies

employees have not been found and spoken to by the quarantine teams, which means they probably left in a hurry to avoid a quarantine (also NW, paywall). References and details in my essay.

2020-06-20 More accurate figures for the Covid-19 associated death toll in GB are available up to about June 5. The UK Office of National Statistics (ONS), an organisation with a world-wide reputation, collects all the data on death certificates, which means also from people who die in care homes and those who die at home, where the certifying medic puts it on the death certificate. The "true" figures are over 60% higher than the daily announced figures by the government. HMG looks to have been identifying in its briefings only about 3/5 of those who died from Covid-19. https://www.theguardian.com/world/2020/jun/19/over-1000-deaths-day-uk-ministers-accused-downplaying-covid-19-peak (I discount the supposed dispute over the figures. It was well-known at the time, to everyone, that HMG was only presenting part of the total in their dail briefings because that is all they had to hand at the time.) I have discussed the figures ONS had started producing in Notes Part 4 on 2020-04-21.

2020-06-24 Woloshin et al consider the accuracy of tests for SARS-CoV-2 infection, with specific focus on the prevalence of false negatives. A false negative could encourage an infected but asymptomatic or paucisymptomatic individual to, say, visit aged grandparents, possibly impairing their continued good health. They consider how specific and sensitive a test needs to be, when considering the posterior risk of infection as compounded from a prior estimate followed by a negative test. Tests with 70% sensitivity can give problematic results ; tests with 90% sensitivity much less so, even when both have 95% specificity. The authors argue that these characteristics of a test should be accurately known, and worry that for many tests they are not https://www.nejm.org/doi/full/10.1056/NEJMp2015897 , published 2020-06-05.

2020-06-24 Ellinghaus et al performed a large genomic analysis study on patients with severe Covid-19 in Spain and Italy and found a locus of genetic susceptibility. https://www.nejm.org/doi/full/10.1056/NEJMoa2020283 , published on 2020-06-17. A blood-group specific analysis showed a higher risk with blood group A that other groups, and a "protective effect" with blood group O.

2020-06-25 Jing et el performed a retrospective cohort study of secondary attack rates in Guangzhou, published in The Lancet Infectious Diseases on 2020-06-17 https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(20)30471-0.pdf The authors considered two kinds of proximity relationships: close family; and same residential address. They calculated the estimated secondary attack rate among household contacts to be 12·4% (95% CI 9·8–15·4) for the relatives cohort and 17·1% (13·3–21·8) for the residential cohort. Age differences were notable: "*[c]ompared with the oldest age group (≥60 years), the risk of household infection was lower in the youngest age group (<20 years; odds ratio [OR] 0·23 [95% CI 0·11–0·46]) and among adults aged 20–59 years (OR 0·64 [95% CI 0·43–0·97]).*" The comment by Pitzer and Cohen is at https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30514-4/fulltext They note in particular that "*only 5% of contacts aged younger than 20 years were infected, which suggests that older age is associated with increased risk of infection conditional on exposure.*" They also note that "[t]*he proportion of identified infections among contacts that were asymptomatic was lower in this study (5%) than [in] estimates from other studies of SARS-CoV-2 (13–18%).*", citing Mitzumoto et al's study of the Diamond Princess https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.10.2000180/ (Erurosurveillance 25(19), 2020-03-10) and Kimball et al on the King County, Washington Care Home outbreak (CDC MMWR April 3) https://www.cdc.gov/mmwr/volumes/69/wr/mm6913e1.htm .

2020-06-28 On Thursday 2020-06-25 there was a press conference on a study by the Medical University of Innsbrück (or Isbruck, as it used to be called when Hendrick Isaac wrote his song at

the end of the 15th century, which JS Bach incorporated into his Johannes Passion, BWV 245) on the February outbreak in Ischgl, in the Austrian alps. The study was led by the virologist Professor Dorothee van Laer. https://science.apa.at/rubrik/medizin_und_biotech/Ischgl-Studie_42_4_Prozent_sind_Antikoerper-positiv/SCI_20200625_SCI39451352255218286 (in German). 79% of the population was tested RT-PCR for existing infection and serologically for past infection. There were 1,473 participants, including 214 children, from 479 households. The seroprevalence lay by 42.4% (in children under 18, it was 27%). It is the highest seroprevalence to be ascertained in any study (those of Vò and of Heinsberg come to mind). It is also well below a level at which herd immunity could occur. Those who tested seropositive without having previously tested positive with a RT-PCR test (that is, who were asymptomative or paucisymptomatic and therefore were not tested) is about 15% of the seroprevalence. Only 9 people, all adults, needed hospitalisation. The study is claiming that its testing is pretty well 100% specificity, with two high-specificity ELISA tests plus further investigation when they rendered different results. The Medical University of Innsbrück's press release is at https://www.i-med.ac.at/pr/presse/2020/40.html

2020-06-28 Guaraldi et al published in The Lancet Rheumatology on 2020-06-24 a retrospective observational controlled cohort study of the use of Tocilizumab in reducing the risk of invasive ventilation or death in severely-ill Covid-19 patients https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30173-9/fulltext Toczilizumab is a monoclonal antibody controlling IL-6 activity, and the hope is to control the cytokine storm with it. About the same proportion of patients required invasive ventilation (18%, compared with 16% in the control group) but Tocilizumab seemed to reduce the chance of death significantly (7% compared with 20% in the control group). Note that the primary outcome of the study was defined as (invasive mechanical ventilation or death) and Schulert notes in his Comment https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30210-1/fulltext that at Day 14 of admission 22.6% of patients had attained the primary outcome, compared with 36.5% in the control.

2020-06-28 Götzinger et al published a multicentre cohort study of children with Covid-19 in The Lancet Child and Adolescent Health on 2020-06-25 https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(20)30177-2/fulltext , studying 582 individuals. 62% were admitted to hospital, 8% requiring intensive care. Four died (CFR 0.69%, 9%% CI 0.20-1.82).

2020-06-28 The US CDC told reporters on 2020-06-24 that, although the number of confirmed Covid-19 cases was near 2.4m, they were seeing about 20 times the seroprevalence than people who had tested positive using RT-PCR. That suggests about 20m Americans have been/are infected. E.g., https://www.theguardian.com/us-news/2020/jun/25/us-coronavirus-cases-count-cdc

2020-06-28 Debby Bogaert is a professor in paediatric infectious diseases at the University of Edinburgh, and one of the "long-haulers", people who suffer symptoms of the disease for many weeks, into some months. https://www.theguardian.com/commentisfree/2020/jun/28/coronavirus-long-haulers-infectious-disease-testing She writes, "*In the last six months, Covid-19 has shown many faces, first causing a high burden of acutely and severely ill patients requiring extensive and intensive care; second being linked with a rare but potentially severe syndrome in children resembling Kawasaki disease; and third a much more common protracted illness among initially mildly infected, and generally young and healthy, adults. This virus is not comparable to a simple flu. Therefore we should focus on suppressing the virus as much as possible, even attempting to eliminate it, while we wait for the development of a vaccine.*"

2020-06-29 UK NICE reviewed evidence for Vitamin D helping to resist Covid-19 infection and found it generally lacking https://www.nice.org.uk/advice/es28/chapter/Factors-for-decision-making

The Scientific Advisory Committee on Nutrition (SACN) came to similar conclusions https://app.box.com/s/g0ldpth1upfd7fw763ew3aqa3c0pyvky The official UK guidance to take 10 µg/day as a supplement remains in place for other reasons and I am still following it.

2020-06-30 A short but poignant opinion by Adam Tooze on the spread of Covid-19 and possibilities for containment https://www.theguardian.com/commentisfree/2020/jun/30/covid-19-global-health-crisis-solutions-americas-india-africa

2020-06-30 it has been a month (2020-05-23, in Notes Part 7) since I gave figures and nominal CFRs for selected countries. Here, from TheG live blog at 0652 BST, are the ten "worst" countries in terms of cases and deaths. Numbers supposedly from JHU Dashboard. I added the remaining countries from previous calculations, below Iran, sometime between 0900 and 1000 UTC. I have added Greece (GR in ISO 3166-2) because of its low numbers, which have surprised some.

I calculated nominal CFR. We are now into enough cases and enough time that a simple division, nominal CFR, is likely to be a good guide to actual CFR.

Country	Cases	Deaths	CFR
Total	10,302,052	505,505	4.90%
US	2,590,552	126,140	4.86%
Brazil	1,368,195	58,314	4.26%
Russia	640,246	9,152	1.43%
India	566,840	16,893	2.98%
GB	313,470	43,659	13.92%
Peru	282,365	9,504	3.36%
Chile	275,999	5,575	2.01%
ES	248,970	28,346	11.38%
IT	240,436	34,744	14.45%
Iran	225,205	10,670	4.73%
FR	201,522	29,816	14.80%
DE	195,042	8,976	4.60%
SE	67,667	5,312	7.85%
BE	61,361	9,732	15.86%
NL	50,433	6,126	12.14%
PT	41,912	1,568	3.74%
PL	34,154	1,444	4.23%
CH	31,652	1,962	6.20%
IE	25,462	1,735	6.81%
AT	17,723	703	3.97%
DK	12,951	605	4.67%
NO	8,862	249	2.81%
FI	7,209	328	4.55%
LU	4,256	110	2.58%
GR	3,390	191	5.63%
IS	1,840	10	0.54%

As has been noted everywhere anytime such figures are mentioned, they include considerable variation in the discovery and logging of the disease and the conditions for logging a death as a Covid-19 death. Someone with symptoms who remains at home and is never tested will not be a “case”; heshe might turn into a “case” later if serologically tested (which may well happen to everyone in many countries before the year is out). Similarly, if few or no post-mortem tests for Covid-19 are carried out, people whose lungs are compromised and who die will not necessarily be logged as Covid-19 deaths, even though they may have been. Similarly, there was a dearth of logging of Covid-19 deaths in care homes in some countries through March, because residents were simply not tested (neither while alive nor post-mortem). Some countries' figures will include all deaths in which Covid-19 involvement is listed on the death certificate (the UK ONS numbers, for example); others will include deaths that are regarded as primarily due to Covid-19 and will not record it if there is a comorbidity involved.The numbers reflect all of these sociological factors.

Having said that, some countries have CFRs above, even well above, 10%. In decreasing order: BE (over 15%), FR (nearly 15%), IT, GB, NL, ES. Some countries have CFR between 5% and 10%: in decreasing order, SE, IE, CH, GR. Most have CFRs above 1% and below 5%. Just one, IS, has a CFR below 1%. Relative position, given by case numbers, has altered a bit: SE has jumped above BE and NL; PT, IE and PL have jumped above CH; PL is now above IE.

Almost all CFR's remain much as they were in late May, but decreased slightly. This phenomenon is expected; early deaths occur to vulnerable people, those with serious comorbidities. What is to explain is why countries' CFRs can be so radically different from each other.

Spain, Italy and France were hit early and hard (early-mid-March), and (some of) their health systems could not at first cope. Also, no standard of care had developed; everything was experimental. GB followed afterwards with peak in late March; so did Belgium. It is being discussed why GB followed that high-case-high-CFR trend, after the situations in IT, FR and ES had become known. It is presumed by some that a week's delay over lockdown was largely responsible (see Notes Part 7, 2020-05-20 entry on James Annan's figures: Notes Part 10, 2020-06-12 entry on Neil Ferguson's evidence to the House of Commons Science and Technology Committee, and Sir David King's interview on the Good Morning Britain show). However, I have seen no discussion of Belgium's comparable curve and comparable CFR.